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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/439,040	11/12/99	VAN DONGEN	J 4222US

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EXAMINER	
WILDER, C	
ART UNIT	**PAPER NUMBER**
1655	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/439,040	Applicant(s) Van Dongen et al.
	Examiner CB Wilder	Group Art Unit 1655

☒ Responsive to communication(s) filed on *Oct 19, 2000*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-12 and 14-21* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-12 and 14-21* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: *EP 97201440.1*.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's amendment filed 10/19/2000 in Paper No. 10 is acknowledged. Claims 1-12 and 17-21 are amended. Claims 1-12 and 14-21 are pending. The arguments have been fully considered but are not found persuasive for the reasons that follows.

This Action is made FINAL.

The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Priority

2. Acknowledgment is made of Applicant's claim for foreign priority based on an application filed in European Patent Office EP 97201440.1 on 05/13/1997. It is noted, however, that a certified copy of the application has not been provided with the instant application serial number 09/439,040 filed 11/12/1999. Therefore, priority once again has not been granted for EP 97201440.1 filing date 05/13/1997.

Previous Objections and Rejections

3. The claim objection drawn to claims 3, 6, 9, 10, 17 and 20 for the British spelling of the term "hybridize" is withdrawn in view of Applicant amendment of the claims. The claim rejection under 35 U.S.C. 112 second paragraph is withdrawn in view of Applicant's amendment of the claims. The claim rejection under 35 U.S.C. 101 drawn to claim 11 is withdrawn in view of Applicant amendment of the claims. The prior art rejection under 35 U.S.C. 102(b) drawn to claims 1-12, 14, 15 and 17-21

as being anticipated by Tkachuk et al. is maintained. The prior art rejection under 35 U.S.C. 102(b) drawn to claim 16 as being anticipated by Rowley et al. is maintained.

Claim Rejections - 35 USC § 102(b)

4. Claims 1-12, 14, 15, and 17-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Tkachuk et al. (Tkachuk, herein) (Science October 1990). Regarding claim 1, Tkachuk discloses a pair of nucleic acid probes having comparable size, said size being from about 10-30 kb in size, and flanking a potential breakpoint in a chromosome, each said probe being labeled with at least one different reporter molecule (page 560, "Figure 1" and col. 1, lines 5-7, 13-15 and 22-27).

Regarding claims 2 and 3, Tkachuk discloses a pair of distinct nucleic acid probes comparable size, said size being from about 10-30 kb and flanking a potential breakpoint in a chromosome, which pair of distinct nucleic acid probes hybridize to a nucleic acid molecule at a genomic distance of less that 250 kb or about 25 to 225 kb (page 560, "Figure 1" and col. 3, lines 2-8). See also *In re Petering*, 301 F.2d 676, 682, 133 USPQ 275, 280 (CCPA 1962)).

Regarding claims 4 and 5, Tkachuk teach wherein the pair of distinct nucleic acid probes are labeled indirectly with at least one reporter molecule and wherein the reporter molecule is a fluorochrome (page 560, col. 1, lines 22-27).

Regarding claims 7-8, and 19-21, Tkachuk teach wherein the distinct nucleic acid probes hybridize to a single corresponding nucleic acid molecule and wherein the single corresponding

nucleic acid molecule is at least a fragment of a chromosome and wherein the chromosome is not aberrant (normal) and aberrant (CML) (page 561, "Figure 3").

Claim 9 is drawn to a pair of nucleic acid probes of claim 1 which hybridize *in situ*. Tkachuk discloses wherein fluorescent *in situ* hybridization was carried out using the probes as described previously (page 560, col. 1, lines 22-27).

Regarding claim 10, Tkachuk discloses wherein the pair of distinct nucleic acid probes hybridizes *in situ* under conditions to only a few linear DNA molecules per cell (page 560, "Figure 1").

Regarding claim 11, Tkachuk discloses a method of detecting a nucleic acid molecule having a chromosomal aberration said method comprising providing a pair of distinct nucleic acid probes to analyze a sample believed to contain nucleic acid (page 559, "Abstract"), said distinct nucleic acid probes having comparable size; said size being from about 10-30 kb in size, and flanking a potential breakpoint in a chromosome, each said probe pair being labeled with at least one different reporter molecule, hybridizing the nucleic acid probe to the nucleic acid; and detecting the presence of the reporter molecule (page 560, "Figure 1" and col. 1, lines 5-7, 13-15 and 22-41).

Regarding claim 12, Tkachuk discloses a method of detecting cells suspected of having a chromosomal aberration, said method comprising providing a pair of distinct nucleic acid probes to analyze nucleic acid of said cells, said distinct nucleic acid probes having comparable size, said size being selected from the group consisting of 10-30 kb in size and flanking a potential breakpoint in a chromosome, each of said pair of distinct probes being labeled with at least one different reporter

molecule; hybridizing said distinct nucleic acid probes to the nucleic acid of at least one if said cells and detecting the presence of said reporter molecule (page 559, col. 3, lines 19-23 and page 560, col. 1, lines 1-3 and 31-41).

Regarding claims 14 and 15, Tkachuk discloses wherein the chromosomal aberration is associated with hematopoietic malignancy (page 559, "Abstract").

Regarding claims 17 and 18, Tkachuk discloses wherein the distinct nucleic acid probes hybridize to a single corresponding nucleic acid molecule and wherein the single chromosome molecule is at least a fragment of a chromosome (page 561, "Figure 3").

Therefore, the claimed invention of claims 1-12, 14, 15, and 17-21 are anticipated by the reference of Tkachuk.

5. Applicant's amendment filed October 19, 2000 (Paper No. 10) has been thoroughly reviewed but they are not found persuasive. Applicant traverses the rejections on the following ground: Applicant argues that "none of the references cited in the Office Action explicitly or inherently teach each of the limitations of any one of the claims pending in the instant application, particularly in light of the claim amendments". Applicant states that Tkachuk et al. do not explicitly or inherently teach each of the limitations included in any one of the rejected claims." Applicant argues that claims 1-10 and 17-21, as amended, each recite a pair of distinct, comparably sized nucleic acid probes which flank a potential breakpoint in a chromosome, and claims 12, 14 and 15 recite methods that require the provision of such probes". Applicant continues by stating that " in contrast, Tkachuk et al. teach the use of a pair of nucleic acid probes which are dissimilar in size (the c-H-able probe being nearly

double in size of the PEM12 probe), and instead of flanking a potential breakpoint in a chromosome, one of the probes of the probe pair taught in Tkachuk et al. PEM12 probe, overlaps the targeted potential breakpoint". Applicant concludes that "as a consequence, Tkachuk et al. do not expressly or inherently teach each of the claimed limitations recited in any one of claims 1-12, 14, 15, or 17-21 and thus respectfully request that the rejection of claims -12, 14, 15 and 17-21 under Section 102(b) be withdrawn".

6. Applicant arguments have been fully considered but they are not found persuasive for the reasons that follows: First, the courts have established that "during patent examination the pending claims must be interpreted as broadly as their terms reasonable allow" *In re Zletz, 893 f. 2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).* In this case, the claims as recited are only limited to a pair of nucleic acid probes having comparable size and flanking a potential breakpoint region of a chromosome and wherein the probes are labeled with a different reporter molecule. The recitation of the probes as being "distinct" does not further limit the claim invention because "distinct" has not been properly defined in the specification or claims and a clear meaning of the term "distinct" as it relates to the claimed probes cannot be determined. Additionally the term "distinct" can be interpreted as meaning "separate" or "discrete" or "notable" or "distinguishable" or etc. Therefore, one ordinary skill in the art would not recognize the metes and bounds of the claim invention. Furthermore, it is clear from the prior Office Action (Paper No. 7) that Tkachuk et al. meets all of the limitations of the claimed invention. As previously noted, Tkachuk et al. teach a pair of nucleic acid probes that are distinguishable or distinct or separate from each other having a size from 18 kb-

35 kb. In contrast to Applicant's arguments, the pair of nucleic acid probes are **not** dissimilar in size because the instant claims recite that the size of the pair of probes can be from 1-100 kb and the probes of Tkachuk et al. fall within that range thus having comparable size as defined by Applicant. Additionally Tkachuk et al. teach wherein the probes flank a potential breakpoint in a chromosome (*See Figure 1*). As noted in the figure, one of the probes is located on one side of the potential breakpoint in the chromosome and the other probe on the other side of the potential breakpoint region. Furthermore, Tkachuk et al. teach that the breakpoint in a chromosome can span multiple regions (exons 2-4) and that one of the probes from the pairs is selected to be telomeric to the breakpoint while the other extends centromeric to the breakpoint cluster region of the chromosome. Tkachuk et al. further teach *in situ* hybridization procedures wherein the distinct nucleic acid probes are utilized therein. It is the Examiner's position that Applicant has not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the reference cited or how the amendments avoid such reference. Accordingly, the prior art rejection under 35 U.S.C. 102(b) drawn to claims 1-12, 14, 15, and 17-21 as being anticipated by Tkachuk et al. is maintained.

7. Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Rowley et al. (Rowley, herein) (5,487,970 January 30, 1996). Claim 16 is drawn to a diagnostic kit comprising at least the pair of nucleic acid probes of claim 1. Rowley teaches a diagnostic kit comprising a pair of nucleic acid probes having comparable size wherein the size is from about 0.3 kb to 1.5 kb, and labels for the

probes for *in situ* hybridization procedures (col. 7, lines 19-44). Therefore, the claimed invention of claim 16 is anticipated by the reference of Rowley.

8. Applicant traverses the rejection on the following grounds: Applicant states that "Rowley et al. teach kits that may include one or more probes". Applicant further argues that "the sequence of the one or more probes may be chosen from four different nucleic acid sequences". Applicant states that "Rowley et al. simply do not teach kits comprising a pair of distinct nucleic acid probes of comparable size and flanking a potential breakpoint in a chromosome". Applicant concludes that "Rowley et al. do not expressly or inherently teach each of the limitations recited in claim 16 and Applicant respectfully request that the rejection of claim 16 under Section 102(b) be withdrawn.

9. These arguments have been fully considered but they are not found persuasive for the reasons that follow: As stated earlier, the courts have established that "during patent examination the pending claims must be interpreted as broadly as their terms reasonable allow" *In re Zletz, 893 f. 2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).* In this case, Rowley et al. meet all of the limitations of the claimed invention. As discussed in the Office Action of Paper No.7, Rowley et al. teach wherein the kit comprises 1 or more than one distinct nucleic acid probes having comparable size as given by the sequence of the probes and in figures 1 and 2. Rowley et al. further teach wherein the cloned DNA probes from both sides of a breakpoint region of a chromosome are used with fluorescent *in situ* hybridization (FISH) to detect translocation in leukemic cells (col. 6, lines 13-16). Rowley et al. state that the kit is used in FISH procedures for detecting translocation in leukemic cells. Therefore, it is the Examiner's position that Applicant has not clearly point out the

patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the reference cited or how the amendments avoid such reference. Accordingly, the prior art rejection under 35 U.S.C. 102(b) drawn to claim 16 as being anticipated by Rowley et al. is maintained.

New Ground(s) of Rejection

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

11. Claims 1-12, 14-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

(a) Claims 1-12, 14-21 are indefinite at the recitation of "distinct" because the term "distinct" has not been defined in the specification or claims and it cannot be determined how the term "distinct" relates to the claimed "nucleic acid probes". Additionally, the term "distinct" is vague and ambiguous and one or ordinary skill in the art would not recognize the metes and bounds of the claimed invention. Clarification is required.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Examiner Cynthia Wilder whose telephone number is (703) 305-1680. The Examiner can normally be reached on Monday through Thursday from 7:00 am to 5:00 pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Exr.'s supervisor, W. Gary Jones, can be reached at (703) 308-1152. The official fax phone number for the Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed the Group's receptionist whose telephone number is (703) 308-0196.

Cynthia B. Wilder

Cynthia B. Wilder, Ph.D.

January 4, 2001

S. Stoner

STEPHEN R. STONER
PRIMARY EXAMINER